GlaxoSmithKline AG

Swiss Summary of the Risk Management Plan (RMP) for Nucala (Mepolizumab)

RMP Summary: Version 6, September 2022
EU RMP: Version 11, 7.7.2022

The Risk Management Plan (RMP) is a comprehensive document submitted as part of the application dossier for market approval of a medicine. The RMP summary contains information on the medicine's safety profile and explains the measures that are taken in order to further investigate and follow the risks as well as to prevent or minimize them.

The RMP summary of Nucala is a concise document and does not claim to be exhaustive.
As the RMP is an international document, the summary might differ from the „Arzneimittelinformation/Information sur le médicament" approved and published in Switzerland, e.g. by mentioning risks occurring in populations or indications not included in the Swiss authorization.
Please note that the reference document which is valid and relevant for the effective and safe use of Nucala in Switzerland is the „Arzneimittelinformation/Information sur le médicament" (see www.swissmedic.ch) approved and authorized by Swissmedic.
GlaxoSmithKline AG is fully responsible for the accuracy and correctness of the content of the here published summary RMP for Nucala.

Summary of risk management plan for Nucala (mepolizumab)

This is a summary of the risk management plan (RMP) for Nucala. The RMP details important risks of Nucala, how these risks can be minimised, and how more information will be obtained about Nucala 's risks and uncertainties (missing information).

Nucala's summary of product characteristics (SmPC) and its package leaflet give essential information to healthcare professionals and patients on how Nucala should be used.

This summary of the RMP for Nucala should be read in the context of all this information including the assessment report of the evaluation and its plain-language summary, all which is part of the European Public Assessment Report (EPAR).

Important new concerns or changes to the current ones will be included in updates of Nucala's RMP.

I. The medicine and what it is used for

Nucala is authorised as an add-on treatment for severe refractory eosinophilic asthma in adult, adolescents and children aged 6 years and older.

Nucala is indicated as an add-on treatment for patients aged 6 years and older with relapsing-remitting or refractory eosinophilic granulomatosis with polyangiitis (EGPA).

Nucala is indicated as an add-on treatment for adult patients with inadequately controlled hypereosinophilic syndrome (HES) without an identifiable non-haematologic secondary cause.

Nucala is indicated as an as add-on therapy with intranasal corticosteroids for the treatment of adult patients with severe chronic rhinosinusitis with nasal polyps (CRSwNP) for whom therapy with systemic corticosteroids and/or surgery do not provide adequate disease control.

See SmPC for further indication information, dose and method of administration.

Further information about the evaluation of Nucala’s benefits can be found in Nucala’s EPAR, including in its plain-language summary, available on the EMA website, under the medicine’s webpage:

http://www.ema.europa.eu/ema/index.jsp?curl=pages/medicines/human/medicines/003860/human_med_001933.jsp&mid=WC0b01ac058001d124

II. Risks associated with the medicine and activities to minimise or further characterise the risks

Important risks of Nucala, together with measures to minimise such risks and the proposed studies for learning more about Nucala's risks, are outlined below.

Measures to minimise the risks identified for medicinal products can be:

- Specific information, such as warnings, precautions, and advice on correct use, in the package leaflet and SmPC addressed to patients and healthcare professionals;

- Important advice on the medicine's packaging;
- The authorised pack size — the amount of medicine in a pack is chosen so to ensure that the medicine is used correctly;
- The medicine's legal status — the way a medicine is supplied to the patient (e.g. with or without prescription) can help to minimise its risks.

Together, these measures constitute *routine risk minimisation* measures.

In addition to these measures, information about adverse reactions is collected continuously and regularly analysed, including PSUR assessment -so that immediate action can be taken as necessary. These measures constitute *routine pharmacovigilance activities*.

If important information that may affect the safe use of Nucala is not yet available, it is listed under 'missing information' below.

II.A List of important risks and missing information

Important risks of Nucala are risks that need special risk management activities to further investigate or minimise the risk, so that the medicinal product can be safely administered. Important risks can be regarded as identified or potential. Identified risks are concerns for which there is sufficient proof of a link with the use of Nucala. Potential risks are concerns for which an association with the use of this medicine is possible based on available data, but this association has not been established yet and needs further evaluation. Missing information refers to information on the safety of the medicinal product that is currently missing and needs to be collected (e.g. on the long-term use of the medicine);

List of important risks and missing information	
Important identified risks	Systemic Reactions including anaphylaxis
Important potential risks	Alterations in immune response (malignancies) Alterations in cardiovascular safety
Missing information	Limited data in pregnant and lactating patients Safety of mepolizumab in children with EGPA Safety of mepolizumab in patients with organ- or life-threatening EGPA

II.B Summary of important risks

Important identified risk: Systemic Reactions including anaphylaxis	
Evidence for linking the risk to the medicine	There have been reports of systemic reactions including anaphylaxis in patients who received mepolizumab. Allergic reactions (including swelling of the face, lips, mouth or tongue; wheezing, difficulty in breathing or shortness of breath; low blood pressure with fainting, dizziness or light headedness; rash; and itchy raised bumps or hives) have been reported in clinical trials with mepolizumab but these reactions have also been reported in people who got an injection of placebo.
Risk factors and risk groups	No risk groups or risk factors were identified during clinical trials in the severe asthma, EGPA, HES and nasal polyps population.
Risk minimisation measures	**Routine risk minimisation measures:** The SmPC includes appropriate information in Section 4.4 (Special Warnings and Precautions) and Section 4.8 (Undesirable effects). Equivalent wording is included in the patient leaflet Section 2 and Section 4. **Additional risk minimisation measures:** None

Important potential risk: Alterations in immune response (malignancies)	
Evidence for linking the risk to the medicine	Certain white blood cell types have been implicated in tumor immune surveillance and the body's ability to fight cancer. The role of eosinophils in this process is unclear. However, since mepolizumab lowers eosinophils, which are a component of innate immunity, cancer is of potential concern in patients taking mepolizumab. The frequency of cancer was monitored in clinical studies with mepolizumab and to date was similar between the patients who received mepolizumab and those who received placebo. The types of cancer were similar to those occurring in general population.
Risk factors and risk groups	No risk groups or risk factors were identified during clinical trials in the severe asthma EGPA, HES and nasal polyps population.
Risk minimisation measures	No risk minimisation measures

Important potential risk: Alterations in cardiovascular safety	
Evidence for linking the risk to the medicine	Effects on the heart and blood vessels were monitored during the studies with mepolizumab. Overall, the effects on the heart and blood vessels were similar between patients receiving mepolizumab and those who received placebo. In one dose-ranging study in patients with severe asthma, effects on the heart occurred more often in patients receiving mepolizumab than those who received placebo. The finding from this study was not seen in other studies in patients with severe asthma, EGPA, HES or nasal polyps.
Risk factors and risk groups	No risk groups or risk factors were identified during clinical trials in the severe asthma EGPA, HES and nasal polyps population.
Risk minimisation measures	No risk minimisation measures

Missing information: Limited data in pregnant and lactating patients	
Risk minimisation measures	**Routine risk minimisation measures:** The SmPC Section 4.6, Fertility, Pregnancy and Lactation, of the SmPC advises prescribers on the non-clinical reproductive toxicity data available on NUCALA. **Additional risk minimisation measures:** None
Additional pharmacovigilance activities	**Additional pharmacovigilance activities:** The Mepolizumab Pregnancy Exposure Study (200870): a VAMPSS post marketing surveillance study of Mepolizumab safety in pregnancy

Missing information: Safety of mepolizumab in children with EGPA	
Risk minimisation measures	**Routine risk minimisation measures:** SmPC Section 4.2, Posology and method of administration, advises prescribers on the dose of mepolizumab for children. **Additional risk minimisation measures:** None
Additional pharmacovigilance activities	**Additional pharmacovigilance activities:** A post-marketing study is proposed to evaluate the safety and efficacy of mepolizumab in children aged 6 – 17 years with EGPA.

Missing information: Safety of mepolizumab in patients with organ- or life-threatening EGPA	
Risk minimisation measures	**Routine risk minimisation measures:** SmPC Section 4.4 Warnings and Precautions, and Section 5.1 Pharmacodymanic properties, advises prescribers on the exclusion of patients with organ-threatening or life-threatening EGPA from the study. **Additional risk minimisation measures:** None
Additional pharmacovigilance activities	**Additional pharmacovigilance activities:** None

II.C Post-authorisation development plan

II.C.1 Studies which are conditions of the marketing authorisation

There are no studies which are conditions of the marketing authorisation or specific obligation of Nucala.

II.C.2 Other studies in post-authorisation development plan

Study 200870 (a VAMPSS post marketing surveillance study of Mepolizumab safety in pregnancy)

Cessation of enrolment to the Mepolizumab Pregnancy Exposure Study, with final closure of study in 2024 See Part **Error! Reference source not found.** for the rationale for cessation of enrolment to study 200870, and Part **Error! Reference source not found.** for continued monitoring of pregnancies and outcomes via routine pharmacovigilance with enhanced data collection. The final report for study 200870 will be available in 2024 as indicated in this RMP (see Part **Error! Reference source not found.**), and this will mark the closure of the study.

EGPA paediatric post-marketing study

A post-marketing study is proposed to evaluate the safety and efficacy of mepolizumab in children aged 6 – 17 years with EGPA. The protocol will be developed and submitted to PRAC within 3 months of European Commission decision for procedure EMEA/H/C/3860/II/36_G.

This summary was last updated in September 2022.